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Quarantine-Based Disease Control in Domesticated Animal Herds

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Abstract—We examine a model of disease control by herd testing and quarantine in domesticated animal herds. Herd status is represented by an integral equation, where the kernel represents the proportion of herds which remain isolated from the general population at a given time after infection is detected. The system steady state, and its local stability are discussed. © 1998 Elsevier Science Ltd. All rights reserved.

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1. INTRODUCTION

Typically, the control of infectious diseases involves two related strategic goals—the isolation of centres of disease to prevent disease spread, and control or eradication within the disease centres themselves. Most models of disease control consider one of these two aspects (for example, [1,2]) but not both. We examine here the stability of a model of infectious disease in domesticated animal herds, where disease control is accomplished by the quarantine of entire herds in which infection is discovered, followed by rigorous "test and slaughter" within infected herds, in an attempt to eradicate it. This model is motivated by the example of bovine tuberculosis (Tb) control in New Zealand cattle herds.

2. MODEL FORMULATION AND ASSUMPTIONS

The disease is assumed to follow two distinct stages, a latent stage and a test reactive stage in which the disease can be detected. The reactive stage contains two substages, the first non-infectious and the second infectious. As we are primarily interested in knowing the proportion of quarantined herds and the epidemiology of disease within the nonquarantined herds, we make

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the following assumptions, which allow us to forego modelling the progress of disease in the quarantined herds, explicitly.

- Quarantine strategy is handled abstractly. All infected animals are removed from the herd before quarantine is lifted. Release of herds from quarantine is modelled through an integral equation with kernel $\phi(\tau)$, where $\phi(\tau)$ is the proportion of herds which remain in quarantine after time τ. Hence, $\phi(\tau)$ is a monotonically decreasing function ≤ 1, for all $\tau > 0$, $\phi(0) = 1$, and $\lim_{\tau \to \infty} \phi(\tau) = 0$. The expected time on infected status is assumed to be a known function, constant in time.
- There is a constant overall number of herds, and number of animals per herd.
- Herds returning from quarantine have a negligible effect on the distribution of infected animals per herd.
- Whole-herd testing is conducted throughout the year; this testing is imperfect and a certain proportion of infected animals will be undetected.
- The proportion of animals per nonquarantine herd in each stage of the disease is determined by the proportion over all nonquarantine herds. While this is unlikely to be true, the only data typically available, and thus, the best measure of the extent of the disease are the number of reactor animals per herd.

3. QUALITATIVE ANALYSIS

We assume that the herds are predominantly disease-free, with occasional multiple case outbreaks or clusters of disease in single herds or localized groups of herds. Outbreaks may, for example, be a result of exceptional contact with external disease sources, or perhaps poor farm management. In all herds, the numbers of diseased animals is expected to be much lower than the total number of animals, with the occasional exception having negligible affect on the disease dynamics. The distribution of infected animals per herd is assumed to follow a negative binomial distribution to allow for clustering of the disease. Distribution parameters k and b define the mean as kb and variance as $kb(1+b)$. The variance to mean ratio, and thus, the value of b is a measure of the dispersion of the data; as $b \to 0$ with constant value of kb, the distribution becomes Poisson.

Consider a system of H herds with constant herd size n. Considering the disease dynamics in all nonquarantine herds, the number of animals/herd in the latent disease stage is l, the number of animals/herd which are test reactors (including those which are both infectious and noninfectious) is r, and the number of infectious animals/herd is i. Then the number of susceptibles is $s = n - l - r$. Primary infection occurs at rate αs and secondary infection at rate $\beta i s$. When a single reactor animal is discovered, the entire herd containing that animal is placed on quarantine, where it is assumed that the infection is eradicated. It is thus necessary to find an expression for the removal to quarantine of animals at all disease stages. With the transfer of herds to quarantine status at rate $g(t)$, reactor animals are transferred at rate $h(t)$; hence, the rate at which latent stage animals are transferred is hl/r and

$$\frac{dl}{dt} = (\alpha + \beta i)(n - l - r) - \gamma l - \frac{l}{r} h(r(t)). \tag{1}$$

We have assumed that infected animals move from the latent stage of the disease to the reactor stage at rate γ, and similarly to the infectious stage at rate η. Then

$$\frac{dr}{dt} = \gamma l - h(r(t)) \tag{2}$$

and

$$\frac{di}{dt} = \eta(r - i) - \frac{i}{r} h(r(t)). \tag{3}$$

If $r(t)$ is known, we can determine the number of infected status herds $I(t)$ and the number of nonquarantine or clear status herds $C(t) = H - I(t)$ by solving the integral equation

$$I(t) = \int_0^\infty \phi(\tau)\,(H - I(t-\tau))\,g(r(t-\tau))\,d\tau. \tag{4}$$

Infection is detected in a herd with x reactor animals, with probability $1 - p^x$, where p is the probability that a single infection will be undetected in a test. If the probability distribution of reactors per herd is $P(x, r(t))$, then the mean probability of detection is

$$g(r(t)) = \sum_{x=1}^{n} P(x, r(t))\,(1 - p^x),$$

and similarly, the mean number of reactor animals removed is

$$h(r(t)) = \sum_{x=1}^{n} P(x, r(t))\,x\,(1 - p^x).$$

Assuming P is negative binomial, then for sufficiently large herd size n and small reactor numbers r, the approximations

$$g(r(t)) \approx \lim_{n\to\infty} g(r(t)) = 1 - K_1^{-(r(t))/b},$$
$$h(r(t)) \approx \lim_{n\to\infty} h(r(t)) = r(t)\left(1 - pK_1^{-(1+(r(t))/b)}\right)$$

can be used, where $K_1 = 1 + b(1-p)$ (see [3], for full development of these expressions).

4. EQUILIBRIUM VALUES AND LOCAL STABILITY OF THE EQUILIBRIUM

The equilibrium value of I is

$$I_\infty = H\frac{\left(1 - K_1^{-(r_\infty/b)}\right)\int_0^\infty \phi(\tau)\,d\tau}{1 + \left(1 - K_1^{-(r_\infty/b)}\right)\int_0^\infty \phi(\tau)\,d\tau}. \tag{5}$$

Setting equations (1)–(3) to zero and eliminating l_∞ and i_∞, we obtain

$$n - r_\infty = \frac{K_2^\infty}{\gamma}\left(r_\infty + \frac{\mu + \gamma + K_2^\infty}{(\alpha/r_\infty) + \beta(\eta/(\eta + K_2^\infty))}\right), \tag{6}$$

which can be solved for r_∞, with $K_2^\infty = 1 - pK_1^{-(1+(r_\infty/b))}$. Hence, $0 < K_2^\infty < 1$. K_2^∞ is a monotonic increasing function of r_∞. A solution to (6) exists and is unique, since the LHS is monotonic decreasing in r_∞ from n to $-\infty$, and the RHS is monotonic increasing from zero to $+\infty$.

The values of l_∞ and i_∞ are easily found once r_∞ is known. Substituting back into (2) and (3) at steady state, we obtain $l_\infty = r_\infty K_2^\infty/\gamma$ and $i_\infty = \eta r_\infty/(\eta + K_2^\infty)$.

Under a perfect testing regime, where every incidence of disease is detected and no secondary transmission occurs (i.e., $p = 0$ and $\beta = 0$),

$$r_\infty = \frac{\gamma\alpha n}{(\alpha+1)(\gamma+1)}.$$

Reduction or elimination of disease thus depends on α. In this case, all steady states are locally asymptotically stable.

4.1. Stability of I_∞

The local stability of the steady state I_∞ is examined through a perturbation, $(I_\infty+\delta I, r_\infty+\delta r)$, occurring at time $t = 0$. We then have

$$I_\infty + \delta I = \int_0^\infty \phi(\tau)\left(1 - K_1^{-(r_\infty+\delta r)/b}\right)(H - I_\infty - \delta I)\,d\tau. \tag{7}$$

Since for $t < 0$, $\delta I(t) = \delta r(t) = 0$,

$$\begin{aligned}\delta I(t) = &-\frac{\ln K_1}{b}(H - I_\infty)K_1^{-(r_\infty/b)}\int_0^t \phi(\tau)\,\delta r(t-\tau)\,d\tau \\ &+ \left(K_1^{-(r_\infty/b)} - 1\right)\int_0^t \phi(\tau)\,\delta I(t-\tau)\,d\tau.\end{aligned} \tag{8}$$

As the stability of r_∞ does not depend on I_∞, let us assume that we have a locally asymptotically stable steady state for r_∞, with the perturbation $\delta r = \sum_j r_j e^{-k_j t}$, where the k_j are positive constants. Then

$$\begin{aligned}\delta I(t) = &-\frac{\ln K_1}{b}(H - I_\infty)K_1^{-(r_\infty/b)}\int_0^t \phi(\tau)\sum_j r_j e^{-k_j(t-\tau)}\,d\tau \\ &+ \left(K_1^{-(r_\infty/b)} - 1\right)\int_0^t \phi(\tau)\,\delta I(t-\tau)\,d\tau.\end{aligned} \tag{9}$$

Taking Laplace transforms,

$$\begin{aligned}\mathcal{L}(\delta I(t)) &= B_0\mathcal{L}\left(\int_0^t \phi(\tau)\sum_j r_j e^{-k_j(t-\tau)}d\tau\right) - B_1\mathcal{L}\left(\int_0^t \phi(\tau)\,\delta I(t-\tau)\,d\tau\right) \\ &= B_0\sum_j \frac{r_j}{s+k_j}\mathcal{L}(\phi) - B_1\mathcal{L}(\phi)\mathcal{L}(\delta I) \\ &= \frac{B_0\mathcal{L}(\phi)}{(1+B_1\mathcal{L}(\phi))}\sum_j \frac{r_j}{s+k_j},\end{aligned} \tag{10}$$

where $-B_0 = (\ln K_1/b)(H - I_\infty)K_1^{-(r_\infty/b)} \le H$, $B_1 = 1 - K_1^{-(r_\infty/b)} \le 1$ and we have used the convolution identity

$$\mathcal{L}(f * g) = \mathcal{L}(f)\,\mathcal{L}(g). \tag{11}$$

The inverse Laplace transform is

$$\mathcal{L}^{-1}(F(s)) = \sum_{\text{all poles}} \operatorname{Res}\left(e^{st}F(s)\right)$$

as long as $F(s)$ has no essential singularities. If $\operatorname{Re}(s) < 0$ for all singularities, the solution is asymptotically stable, while if for at least one pole $\operatorname{Re}(s) \ge 0$, the stability of the solution is undetermined. Now since the k_j are positive, the stability of the solution is dependent on the form of $\phi(t)$. Where all herds return from quarantine after a fixed period τ_m,

$$\phi_1(t) = 1 - u(t - \tau_m), \tag{12}$$

where u is the Heaviside function. The Laplace transform for ϕ_1 is $(1/s)(1 - e^{-\tau_m s})$ so that

$$\mathcal{L}(\delta I_1(t)) = \frac{B_0(1 - e^{-\tau_m s})}{(s + B_1(1 - e^{-\tau_m s}))}\sum_j \frac{r_j}{s+k_j}, \tag{13}$$

and the only purely real singularities occur at $s = -k_j$. Complex singularities are determined by the solution of the simultaneous set of equations

$$s_R + B_1\left(1 - e^{-\tau_m s_R}\cos\left(\tau_m s_I\right)\right) = 0,$$
$$s_I + B_1 e^{-\tau_m s_R}\sin\left(\tau_m s_I\right) = 0,$$

where s_R and s_I are the real and imaginary parts of s, respectively. Isolating the trigonometric terms on one side of the equation, squaring both sides and adding the two equations leads to the expression

$$\left(s_R + B_1\right)^2 + s_I^2 = B_1^2 e^{-2\tau_m s_R}. \tag{14}$$

This equation has no solution for $s_R > 0, \tau_m > 0$, therefore, all singularities must lie in the left half of the complex plane (the solution at $s_R = 0$ is not a singularity for $\mathcal{L}(\delta I_1(t))$, by L'Hôpital's rule), and $\lim_{t\to\infty} \delta I_1(t) = 0$. Consider now some $\phi_2(t)$, such that

$$\phi_2(t) \le \phi_1(t), \qquad \forall t > 0.$$

For a perturbation of fixed magnitude occurring at time $t = 0$, let the time evolution be δI_i under the kernel ϕ_i. Then for $\epsilon \ll 1$, we have to first order,

$$\begin{aligned}\delta I_2(\epsilon) &\approx B_0\left(\phi_2(0)\,\delta r(\epsilon) + \phi_2(\epsilon)\,\delta r(0)\right) + \frac{\epsilon}{2}\left(\phi_2(0)\,\delta I_2(\epsilon) + \phi_2(\epsilon)\,\delta I_2(0)\right)\\ &= \left(\frac{\epsilon}{2 - \epsilon\phi_2(0)}\right)\left[B_0\left(\phi_2(0)\,\delta r(\epsilon) + \phi_2(\epsilon)\,\delta r(0)\right) + \phi_2(\epsilon)\,\delta I_2(0)\right]\\ &\le \delta I_1(\epsilon).\end{aligned}$$

Since the location of the origin in time is arbitrary, then if the perturbation under ϕ_1 is the same as under ϕ_2 at any given time $t = t_p$, then $\delta I_1 > \delta I_2$, for all time $t > t_p$. Therefore, if r_∞ is locally asymptotically stable, then for all allowable ϕ_i, I_∞ is also locally asymptotically stable.

4.2. Stability of the Infection Stages

For the stability of the steady state of the infection, the perturbation equations about the steady state $(l_\infty, r_\infty, i_\infty)$ of equations (1)–(3) can be written,

$$\frac{d}{dt}\begin{pmatrix}\delta l\\ \delta r\\ \delta i\end{pmatrix} = \mathbf{J}\begin{pmatrix}\delta l\\ \delta r\\ \delta i\end{pmatrix}, \tag{15}$$

where

$$\mathbf{J} = \begin{pmatrix} -\alpha - \mu - \beta i_\infty - \gamma - K_2^\infty & -\alpha - \beta i_\infty - \dfrac{l_\infty}{b}K_2^\infty & \beta\left(n - l_\infty - r_\infty\right)\\ \gamma & -K_2^\infty - \dfrac{r_\infty}{b}\left(1 - K_2^\infty\right) & 0\\ 0 & \eta - \dfrac{i_\infty}{b}\left(1 - K_2^\infty\right) & -\eta - K_2^\infty \end{pmatrix} \tag{16}$$

is the Jacobian matrix for equations (1)–(3). The characteristic equation can be written as

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \tag{17}$$

where

$$
\begin{aligned}
a_1 &= -(J_{11}+J_{22}+J_{33}) = \alpha+\gamma+\eta+3K_2^\infty+\frac{r_\infty}{b}L_\infty+\beta i_\infty,\\
a_2 &= J_{11}J_{22}+J_{11}J_{33}+J_{22}J_{33}-J_{21}J_{12}\\
&= (\alpha+\gamma+\beta i_\infty+K_2^\infty)\left(K_2^\infty+\frac{r_\infty}{b}L_\infty\right)+(\alpha+\gamma+\beta i_\infty+K_2^\infty)(\eta+K_2^\infty)\\
&\quad+\left(K_2^\infty+\frac{r_\infty}{b}L_\infty\right)(\eta+K_2^\infty)+\gamma\left(\alpha+\beta i_\infty+\frac{l_\infty}{b}L_\infty\right),\\
a_3 &= J_{21}J_{12}J_{33}-J_{21}J_{13}J_{32}-J_{11}J_{22}J_{33}\\
&= \gamma\left(\alpha+\beta i_\infty+\frac{l_\infty}{b}L_\infty\right)(\eta+K_2^\infty)-\gamma\beta(n-l_\infty-r_\infty)\left(\eta-\frac{i_\infty}{b}L_\infty\right)\\
&\quad+(\alpha+\gamma+\beta i_\infty+K_2^\infty)\left(K_2^\infty+\frac{r_\infty}{b}L_\infty\right)(\eta+K_2^\infty),
\end{aligned}
$$

and $0 < L_\infty = K_1^{-(1+(r_\infty/b))} < 1$ has been adopted for notational convenience. Recall that the Routh-Hurwitz criteria gives the necessary and sufficient conditions for eigenvalues with negative real part (and thus local asymptotic stability):

$$a_1 > 0, \tag{18}$$

$$a_3 > 0, \tag{19}$$

$$a_1a_2 - a_3 > 0. \tag{20}$$

Clearly, a_1 and a_2 are both strictly positive. If $a_3 < 0$, then all eigenvalues are real, and the system is locally unstable. This can only occur if

$$\eta > \frac{i_\infty p}{b}K_1^{-(1+(r_\infty/b))}.$$

If $a_3 > 0$, then a Hopf bifurcation may occur when $a_1a_2 = a_3$, however, the analysis lies outside the scope of this paper.

We have derived expressions for the steady state and local stability of the distribution of disease, with a herd of domesticated animals. The application of these results to the control of tuberculosis in cattle is discussed in [3].

REFERENCES

1. P. van den Driessche, Some epidemiological models with delays, In *Differential Equations and Applications to Biology and Industry*, (Edited by M. Martelli, K. Cooke, E. Cumberbatch *et al.*), pp. 507–520, World Scientific, Singapore, (1996).
2. T.J. Ryan, A spreadsheet model of tuberculosis control, *The Kenya Veterinarian* **18** (2), (1994).
3. R.R. Kao, M.G. Roberts and T.J. Ryan, A model of bovine tuberculosis control in domesticated cattle herds, *Proceedings of the Royal Society of London, Series B*, (submitted).